

CLAIMS

What is claimed is:

1. A CD28 peptide mimetic for blocking deleterious T cell mediated immune reaction,
said peptide mimetic being from 15 to 30 amino acids in length,
said peptide mimetic comprising levorotary or dextrorotary amino acids,
said peptide mimetic comprising a core motif dispersed between two flanking
sequences, each of said flanking sequences comprising a plurality of amino acids;
wherein the sequence of the core motif is MYPPPY, SEQ ID NO. 1, when the
peptide mimetic comprises levorotary acids;
wherein the sequence of the core motif is YPPPYM, SEQ ID NO. 2, when the
peptide mimetic comprises dextrorotary acids; and
wherein the peptide mimetic assumes a polyproline conformation when placed in
water at physiological pH and a temperature of about 25° C.
2. The peptide mimetic of claim 1 wherein the flanking sequences are amphiphilic,
anti-parallel, right-twisted B strands and charged amino acid residues.
3. The peptide mimetic of claim 1 wherein the amino and carboxyl ends of the
peptide are end blocked.
4. The peptide mimetic of claim 1 wherein the peptide mimetic binds to the B71
ligand with an affinity that is from 10 fold greater to 2 fold less than CD 28.
5. The peptide mimetic of claim 1 wherein the affinity of the peptide mimetic for the
B71 ligand is less than the affinity of CTLA-4 for the B71 ligand.
6. The peptide mimetic of claim 1 wherein the Kd of the mimetic with respect to
B71 is from 2 to 3 micromoles.

7. The peptide mimetic of claim 1 wherein the flanking sequences of the L form of the peptide mimetic comprises a repetitive LS sequence, and wherein the flanking sequence of the D form of the peptide mimetic comprises a repetitive SL sequence.

8. The peptide mimetic of claim 1 wherein said peptide mimetic comprises the sequence of SEQ ID NO. 3.

9. The peptide mimetic of claim 1 wherein said peptide mimetic comprises the sequence of SEQ ID NO. 4.

10. The peptide mimetic of claim 1 wherein said peptide mimetic comprises SEQ ID NO. 5 or SEQ ID NO. 6.

11. The peptide mimetic of claim 1 wherein said peptide mimetic comprises SEQ ID NO. 7 or SEQ ID NO. 8.

12. The peptide mimetic of claim 1 wherein said peptide mimetic comprises SEQ ID NO. 9 or SEQ ID NO. 10.

13. The peptide mimetic of claim 1 wherein said peptide mimetic is a biologically active variant of a peptide mimetic which comprises one of the following reference sequences: SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9 or SEQ ID NO. 10; and

wherein the sequences which flank the core motif of the variant are at least 70% identical with the sequences which flank the core motif in one of said reference sequences.

14. The peptide mimetic of claim 13 wherein the sequence which flank the core motif of the variant are at least 80% identical with the sequences which flank the core motif in one of said reference sequences.

15. The peptide mimetic of claim 13 wherein the sequence which flank the core motif of the variant are at least 90% identical with the sequences which flank the core motif in one of said reference sequences.

5 16. The peptide mimetic of claim 13 wherein said peptide is from 17 to 25 amino acids in length.

17. A method of treating a subject with a T cell mediated disorder or autoimmune disease comprising: administering a biologically effective amount of one or more CD 28
10 peptide mimetics of claim 1 to said subject.

18. The method of claim 17 wherein the subject has multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, or has received or is about to receive an allograft transplant.

15 19. The method of claim 17 wherein the sequences which flank the core motif of the peptide mimetic are amphiphilic, anti-parallel, right-twisted B strands and charged amino acid residues.

20 20. The method of claim 17 wherein the amino and carboxyl ends of the peptide are end blocked.

21. The method of claim 17 wherein the peptide mimetic binds to the B71 ligand with an affinity that is from 10 fold greater to 2 fold less than CD 28.

25 22. The method of claim 17 wherein the affinity of the peptide mimetic for the B71 ligand is less than the affinity of CTLA-4 for the B71 ligand.

23. The method of claim 17 wherein the Kd of the mimetic with respect to B71 is
30 from 2 to 3 micromoles.

24. The method of claim 17 wherein said peptide mimetic comprises the sequence of SEQ ID NO. 3, or the retro inverso isomer thereof.

25. The method of claim 17 wherein said peptide mimetic comprises the sequence of
5 SEQ ID NO. 4.

26. The method of claim 17 wherein said peptide mimetic comprises SEQ ID NO. 5 or SEQ ID NO. 6.

10 27. The method of claim 17 wherein said peptide mimetic comprises SEQ ID NO. 7 or SEQ ID NO. 8.

28. The method of claim 17 wherein said peptide mimetic comprises SEQ ID NO. 9 or SEQ ID NO. 10.

15 29. The method of claim 17 wherein said peptide mimetic is a biologically active variant of a peptide mimetic which comprises one of the following reference sequences: SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9 or SEQ ID NO. 10; and

20 wherein the sequences which flank the core motif of the variant are at least 70% identical with the sequences which flank the core motif in one of said reference sequences.

30. The method of claim 17 wherein said peptide mimetic is from 17 to 25 amino
25 acids in length.

31. The method of claim 1 wherein the flanking sequences of the L form of the peptide mimetic comprises a repetitive LS sequence, and wherein the flanking sequence of the D form of the peptide mimetic comprises a repetitive SL sequence.

32. A method of blocking activation and proliferation of CD4⁺ cells comprising contacting such cells with one or more CD 28 peptide mimetics of claim 1.